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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,626	06/05/2001	Johanna Jacoba Maria Meulenberg	4041.1US	9761

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EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 12/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,626	MEULENBERG ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-22* is/are pending in the application.

4a) Of the above claim(s) *1-4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 10-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). ← 09/297585

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election of Group III (claims 5-7 and 20-22) in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In view of the amendments to the claims, the prior restriction requirement is withdrawn and the following restriction requirement is set forth:

Group I, claims 1-4 drawn to a method of making an infectious RNA clone.

Group II, claims 5-7 and 10-22 drawn to a recombinant RNA virus.

Because of the election of Group III, now part of Group II in view of the claim amendments, claims 5-7 and 10-22 are under consideration in the instant office action.

Applicant is advised that a rejoinder of claims is possible at a later date if the product is eventually found patentable. Guidance on treatment of product and process claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b) is set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86.

> To facilitate examination under § 103, where product and process claims are presented in the same application, applicant may be called upon under 35 U.S.C. § 121 to elect claims to either the product or process. The claims to the non-elected invention will be withdrawn from further consideration. However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 3, is attached to the instant Office Action.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892 or they have been listed by applicant on the PTO-1449 form, they have not been considered.

Drawings

The drawings are objected to, please see Notice of Draftsperson's Review attached to the instant Office Action. Correction is required.

Claim Objections

Claim 13 is objected to because of the following informalities: The claim uses the abbreviation PPRSV the compounds should be spelled out before the first use of the abbreviation. Appropriate correction is requested.

Claim 10 is objected to because of the following informalities: The claim is dependent on a claim from a non-elected invention. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-7 and 11-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 5-7 and 11-22 the term "a modified RNA virus" is indefinite, because the ordinary artisan would not know the metes and bounds of this term. How much of the virus needs to be modified in order to fall within the scope of being modified. Inserting a gene sequence in an expression vector modifies the original sequence by deleting or inserting a few nucleotides. "Modified" can also be interpreted to mean simply changing the environment, for instance purifying the virus particles from tissue culture. Therefore, unless the term is specifically defined, any manipulation of the RNA virus will suffice to fall within the scope of being "modified".

In claim 20 the term "a derivative of either" is indefinite, because the ordinary artisan would not know the metes and bounds of this term in combination with the term "a full-length DNA copy". How much of the virus needs to be modified in order to fall within the scope of being "a derivative of either". The claim rejection may be overcome by clarification of the

meaning "a derivative of either" or by deleting the entire section "a derivative of either said at least one DNA copy or said at least on in-vitro transcribed copy".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Frolov et al. (PNAS 1996).

The instant invention is drawn to "a modified" RNA virus comprising recombinant nucleic acids, a vaccine and a cell infected with the modified RNA virus. The specification does not clearly define what is encompassed by "a modified" RNA virus, therefore, removing the virus from its natural setting, isolating it from other proteins, manipulating it in any way would fall with the scope of modification. Recombinant DNA or recombinant nucleic acid can be interpreted to mean sequences from different sources or manipulating the sequences in any way by well-known laboratory techniques.

Frolov et al. teaches an alphavirus based expression vector. Alphavirus are positive stranded RNA viruses. The reference teaches producing virions by *in vitro* transcription of the RNA (see figure 1). The reference teaches expressing heterologous sequences from the alphavirus vector (see figure 4). The reference also teaches the use of these expression vectors as

a vaccine (see page 11376, column 1, paragraph 2). Therefore, the instant invention is anticipated by Frolov et al.

Claims 5, 6, 7 are rejected under 35 U.S.C. 102(b) as being anicipated by Moormann et al. (Journal of Virology 1996).

The instant invention is drawn to "a modified" RNA virus comprising recombinant nucleic acids, a vaccine and a cell infected with the modified RNA virus. The specification does not clearly define what is encompassed by "a modified" RNA virus, therefore, removing the virus from its natural setting, isolating it from other proteins, manipulating it in any way would fall with the scope of modification. Recombinant DNA or recombinant nucleic acid can be interpreted to mean sequences from different sources or manipulating the sequences in any way by well-known laboratory techniques.

Moorman et al. discloses a method of obtaining an infectious RNA virus by *in vitro* translating cDNA. The reference describes the complete cDNA sequence of the C strain (a vaccine strain) of the classical swine fever virus. The reference teaches the construction of a full-length DNA copy of this sequence from which infectious RNA was transcribed. In addition, the infectious copy was used to construct a hybrid virus in which the 5' half of the E2 gene was replaced by the equivalent region from CSFV strain Brescia (see page 768, column 2, 3rd paragraph). Therefore, the present invention is anticipated by Moorman et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-7 and 10-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wensvoort et al (WO 92/21375) in view of Moormann et al. (J. of Biol. Chem. 1996).

The instant invention is directed to a recombinant nucleic acid sequence of a virus belonging to the order *Nidoviralis*. The cDNA is *in vitro* transcribed nucleic acids produces an infectious RNA. In addition the recombinant cDNA and subsequent infectious RNA is modified to contain the ORF of another *Arteviradae* family member. Claims 10 and 20 are interpreted as a product for this office action, the preamble of the product by process were interpreted as "a composition of matter" (which are products). Product by process claims are not limited to the

manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113 states that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

The reference of Wensvoort et al. teaches the nucleic acid sequence of Leystad virus (LV)which belongs to the order *Nidoviralis* (see figure 1). The genome of LV is 14.5 to 15.5 in length (see page 7, lines 15-22). The refence teaches using the protein products for the development of vaccines (see page 8, lines 3-9) and diagnostic agents (see page 9, lines 3-29). The reference contemplates using recombinant virus constructs as a vaccine (page 11, lines 6-22, and claims 4, 9 and 10). The open reading frame ORF-7 is translated from a small subgenomic RNA having its own leader sequence, indicating that this ORF is independent of the others. The reference does not teach *in vitro* transcribing the cDNA to produce an infectious RNA clone.

The reference of Moormann et al. teaches *in vitro* transcribing cDNA from a positive stranded RNA virus to produce an infectious clone. The reference also teaches replacing the ORF of one virus with the ORF of another strain of virus. Replacing these heterologous nucleic acid sequences produces a virus that can be used as a vaccine, and this vaccine virus can be distinguished from a natural infection by the different antigens it presents. The reference does not teach making an infectious clone of PPRSV.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the cDNA taught by Wenvoort et al. and apply the *in vitro* method taught by

Moorman et al. to produce an infectious RNA particle. One of ordinary skill in the art would have been motivated to use an *in vitro* transcribed virus, for the purpose of vaccination because the composition is completely defined. One of ordinary skill in the art would have been motivated to produce a vaccine that contains heterologous sequences in order to have a marker that can distinguish vaccinated from naturally infected animals. Exchanging open reading frame sequences from viruses that are closely related would have the expectation that the virus is able to function as it would normally. Therefore, the instant invention is obvious over Wensvoort et al. in view or Moormann et al.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. U.S. Pat. No. 5,620,691.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D. 12/11/02